



The Strategic Playbook Series

Eli Lilly:

Leading the GLP-1 Market with Scale, Growth, and Strong Margins

Executive Summary

Three Core Pillars of the Eli Lilly (LLY) Investment Thesis

Eli Lilly Company Overview

- **Global market cap leader (>US\$1,058bn), fastest-growing, and highest-margin multinational biopharmaceutical major.** Flagship incretin franchises account for 67% of 2026E total revenue.
- **Global GLP-1 Category Leader (2Q26 Global / US Share: 55% / 61%):** Leveraging its breakthrough dual GIP/GLP-1 receptor agonist Tirzepatide (Mounjaro for T2D / Zepbound for Obesity), LLY has demonstrated generational clinical superiority over legacy single-target agents. Backed by >US\$20bn in manufacturing capex and direct-to-consumer access via LillyDirect, LLY has established clear global category leadership.
- **Constructing a High-Margin, Diversified, and Sustainable Global Commercial Platform:** Next-generation blockbuster pipeline—including Donanemab (Alzheimer's), Orforglipron (oral small molecule), and Retatrutide (triple agonist)—expands LLY's platform from pure metabolic control into broad preventive medicine across cardiovascular, respiratory, and neurodegenerative diseases.

Three Primary Investment Pillars

- **GLP-1 Category Leadership:** Global GLP-1 market projected at 12.4% 5-year CAGR; global treated patient pool doubling over the next 5 years; immediate volume tailwinds from the US Medicare Bridge program (effective 2026.07.01).
- **Next Growth Engine, GLP-1 3.0 Pipeline Driving Patient Migration:** Tirzepatide (Mounjaro/Zepbound) anchors core cash flows (65% of 2026E sales); Orforglipron (oral small molecule; April 2026 launch) penetrates mass and primary-care markets; Retatrutide (Phase 3; 2027–28E launch) sets the efficacy ceiling. Together, they secure patient migration ahead of Dulaglutide (Trulicity) Loss of Exclusivity (LOE) in late 2027.
- **Financial Visibility & Compelling Valuation:** Fastest growth among pharma majors (2027E EPS +33% YoY; 2025–30E CAGR 23.5%), industry-leading operating margins and ROE, net cash balance sheet. Currently trades at 23.8x 2027E P/E and 1.9x PEG (a marked discount to global mega-cap tech at 2.4x).

The GLP-1 Landscape: Transitioning from Injectable to Oral, 1.0 to 3.0

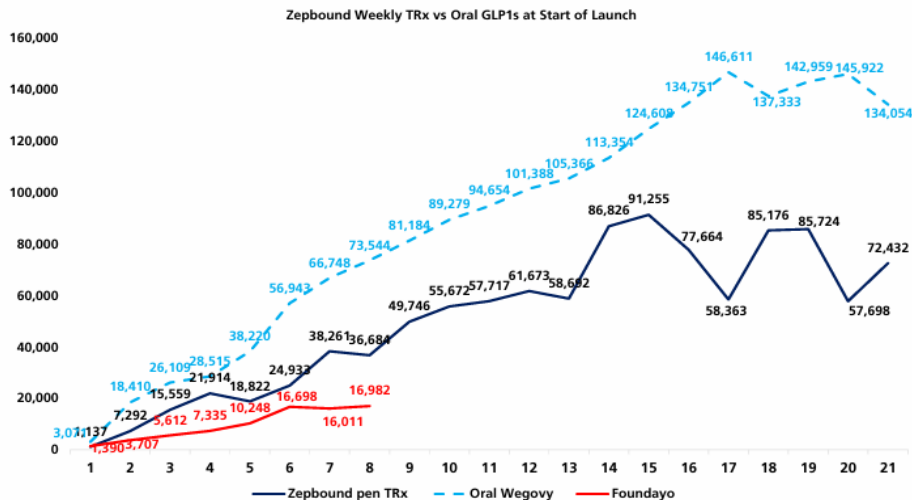
NVO and LLY are the GLP1 market leaders with Wegovy/Ozempic and Mounjaro/Zepbound – which are weekly injections



NVO has an oral version of Wegovy approved as of Dec 2025 and LLY also now recently launched Foundayo as of April 2026



Orals are off to a decent start but not expected to be game changing in the near term in the US as injectables are likely to be used more given superior efficacy



What Is GLP-1? Mechanism of Action

Dual Central & Gastrointestinal Pathways Suppress Appetite and Prolong Satiety

GLP-1 (glucagon-like peptide-1) is an endogenous hormone secreted by the gut after eating, and **GLP-1 agents** mimic this natural hormone to deliver both precise glycaemic control and significant weight loss.

1. Central neural regulation: reduces food "noise" and suppresses appetite

- **Hypothalamic Appetite Center:** GLP-1 crosses the blood–brain barrier and acts directly on the hypothalamus, activating anorexigenic neurons (POMC/CART), while inhibiting hunger-promoting neurons (NPY/AgRP), causing the brain to signal satiety.
- **Mesolimbic Reward System:** Acts on dopamine reward circuits, markedly reducing psychological cravings for high-fat, high-sugar and other calorie-dense foods (clinically described as eliminating "food noise"), and suppressing emotional eating and snacking impulses.

2. Gastrointestinal motility: delays gastric emptying

- **Prolongs Physical Satiety:** GLP-1 suppresses gastric motility, substantially prolonging food retention and digestion time in the stomach.
- **Reduces Meal Size:** Because the stomach remains persistently filled, patients experience strong gastric fullness after consuming far less than usual, naturally reducing daily calorie intake.

3. Metabolism and glycaemic stability: blocks "pseudo-hunger"

- **Metabolic Homeostasis:** Glucose-dependent insulin stimulation and glucagon suppression prevent postprandial glucose crashes that trigger reactive hunger and sugar cravings.

4. Multi-Target Evolution: Dual & Triple Agonism

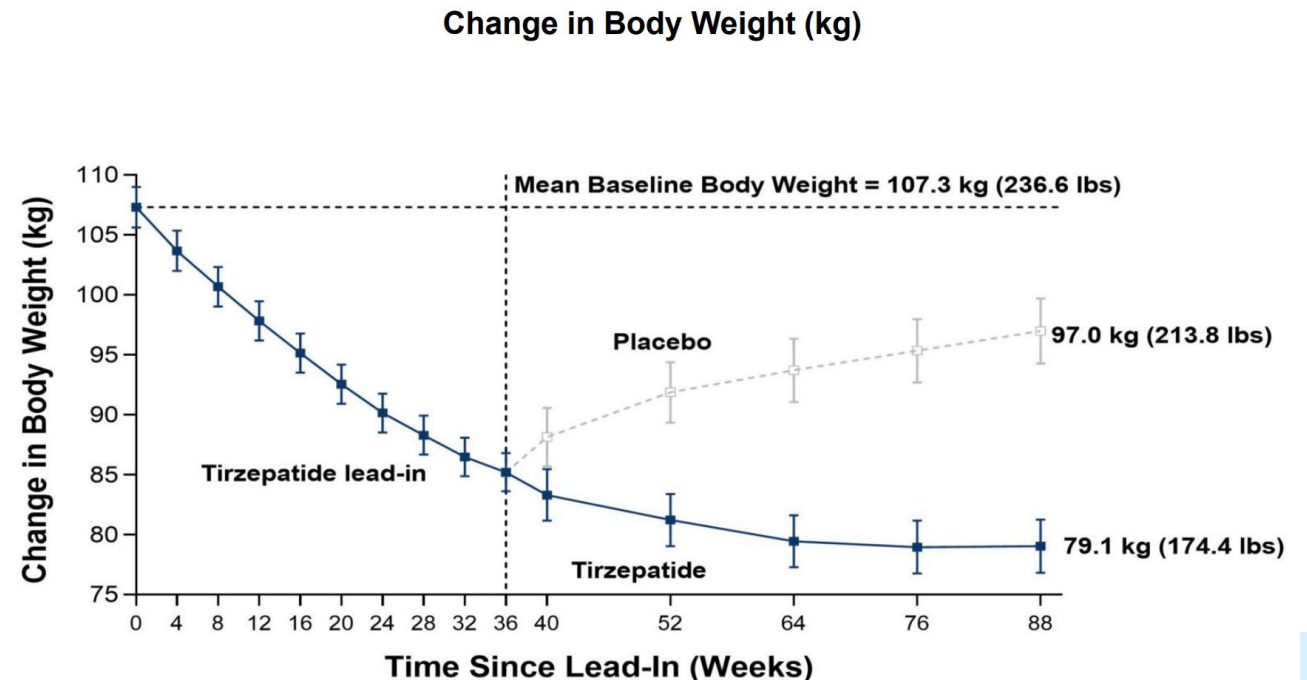
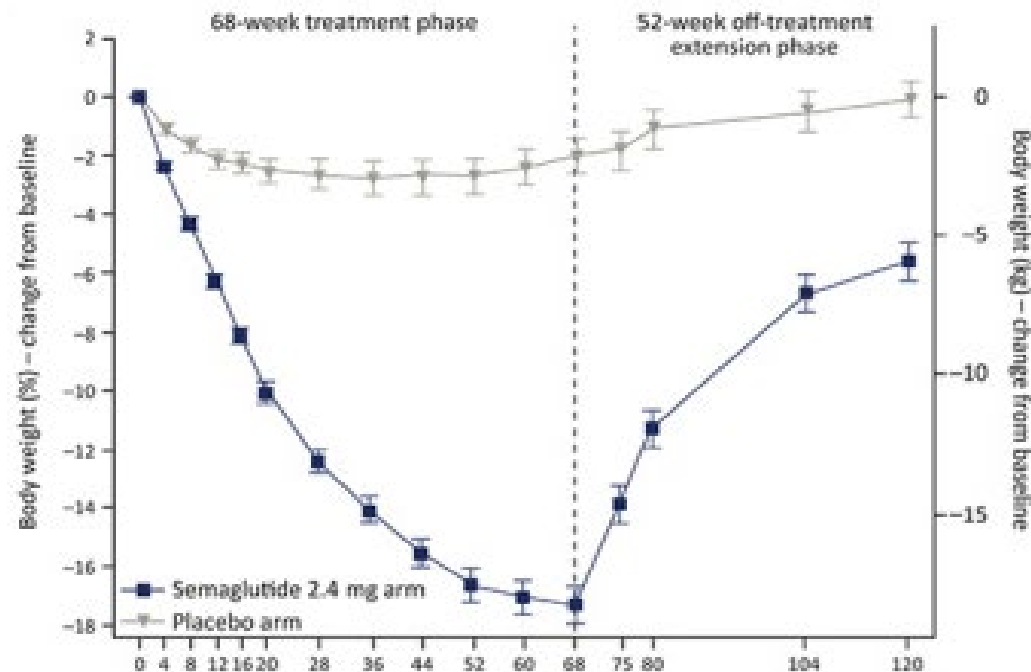
- **+ GIP (Dual Agonist):** GIP improves lipid storage and insulin sensitivity in adipose tissue, and GLP-1 synergizes in the brain to further amplify appetite suppression.
- **+ Glucagon (Triple Agonist 'GGG'):** Glucagon receptor agonism directly stimulates hepatic lipid beta-oxidation, and increases basal metabolic rate (Energy Expenditure), breaking the metabolic compensation and weight-loss plateau of simple "eating less".

What Is GLP-1? The Chronic Nature of Incretin Therapy

Ongoing treatment and lifestyle synergy are essential for long-term metabolic control.

GLP-1/Incretin - Significant Weight Regain Post-Discontinuation:

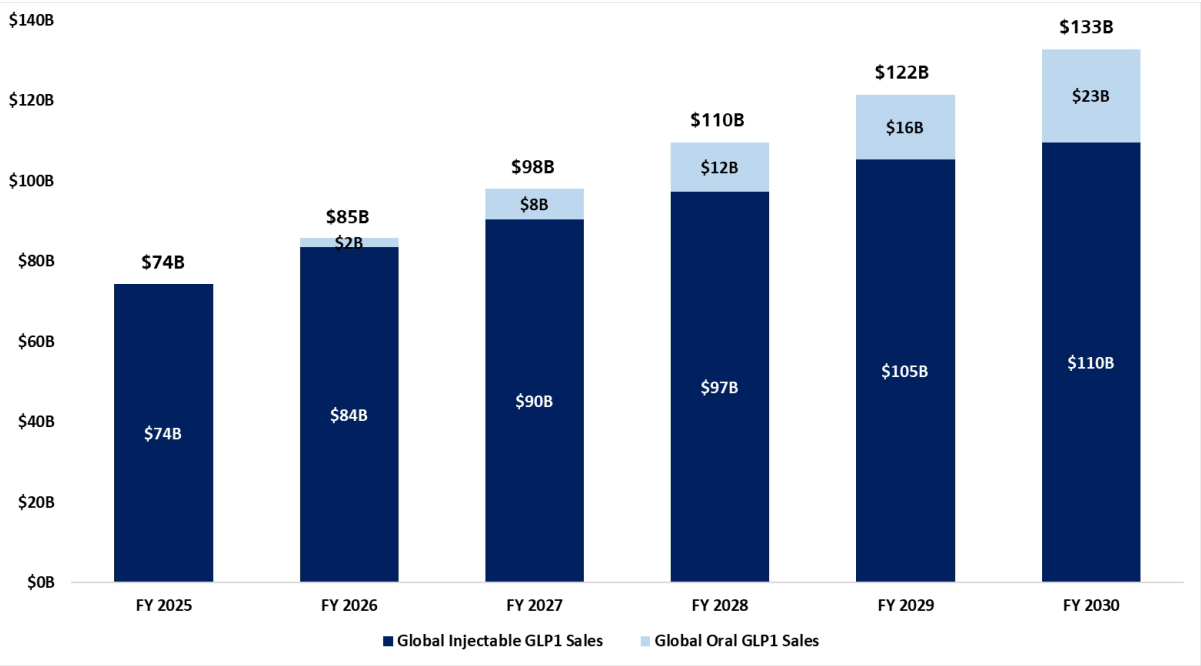
- **Semaglutide (Wegovy):** Following cessation, patients regained on average approximately 12 percentage points, about 2/3;
- **Tirzepatide (Zepbound/Mounjaro)** After switching to placebo, within 52 weeks, experienced an average weight regain of about 14%, and only about 17% were able to maintain at least 80% of their initial weight loss; by comparison, those continuing tirzepatide retained 90%.
- **Real-World Persistence Challenges:** 1-year discontinuation reaches ~65% in non-diabetic obesity and ~45% in T2D. The commercial and clinical success of weight-loss drugs depends not only on initial weight-loss magnitude but also on patients' ability to afford, tolerate, and remain on long-term therapy.



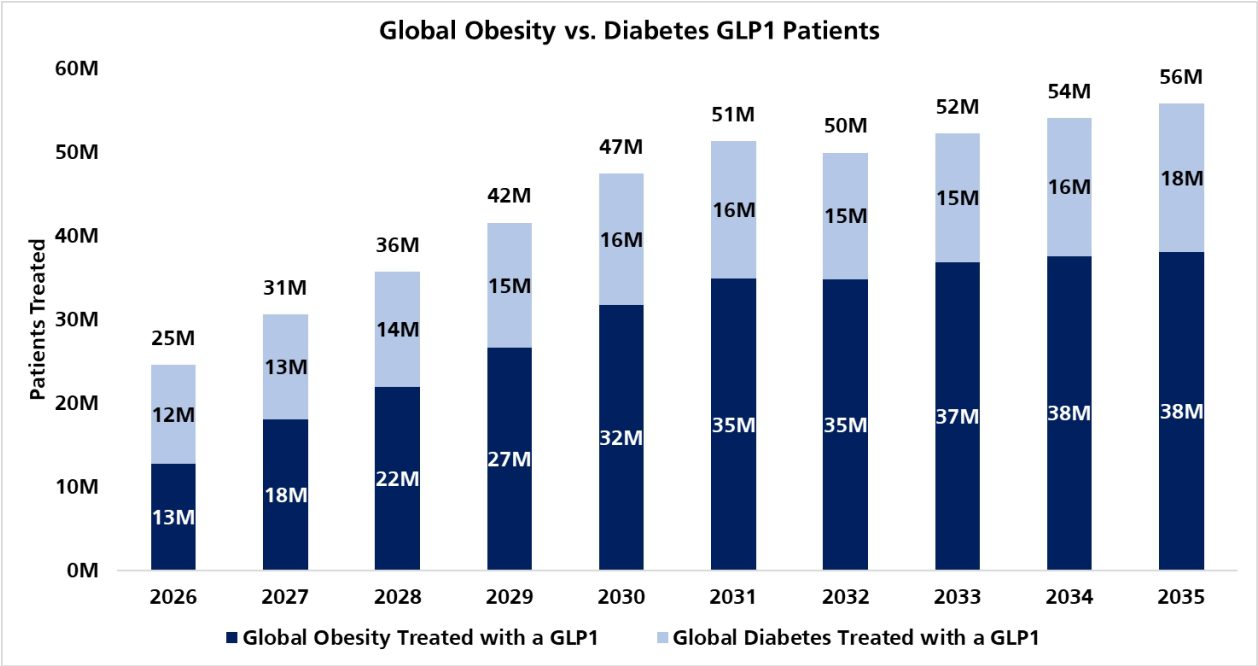
Global Incretin Market: 12.4% 5-Year CAGR, Treated Population Doubling

Obesity therapeutics driving market expansion

The market is currently dominated by injectables. Oral formulations are projected to capture ~20% market share by 2030E, when the global market is expected to reach US\$133bn (Surpassing global energy drink and ice cream categories).



Driven by expanded clinical obesity management, the global treated patient population will double to over 56 million individuals.

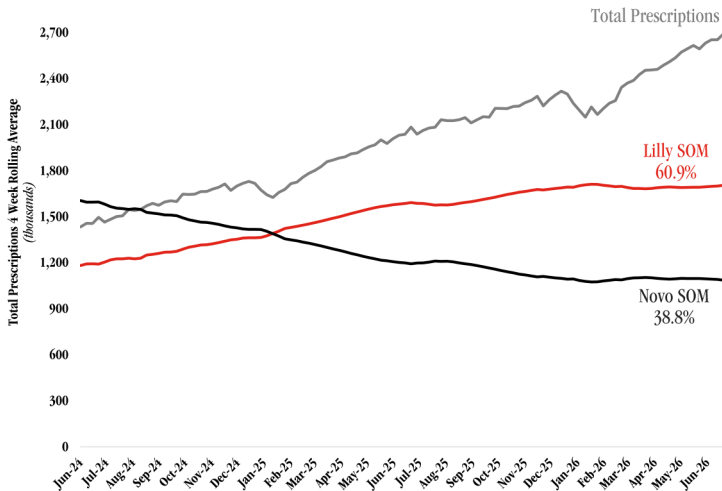


Eli Lilly vs Novo Nordisk: The Global Incretin Duopoly

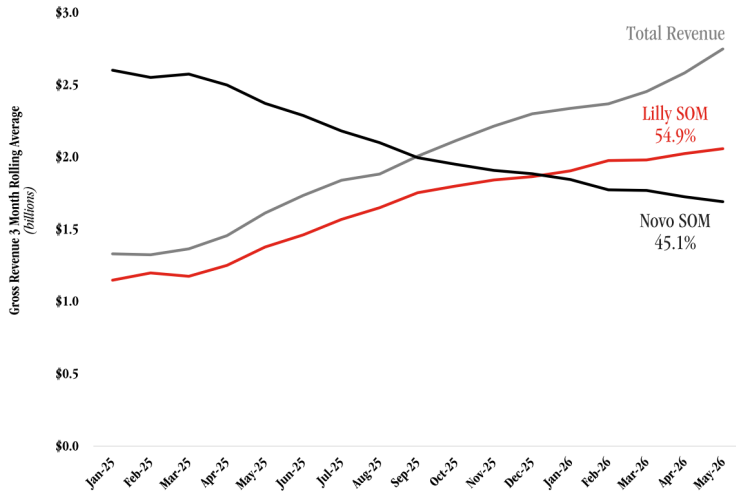
Novo Nordisk pioneered the class (1st-Gen in 2014); Eli Lilly has established undisputed global leadership.

Region / Period	Market-share calculation basis	Eli Lilly	Novo Nordisk	Key definitions
US 2026 Q2	Prescription volume (TRx); four-week rolling average, through 26 June 2026 weekly data	60.9%	38.8%	Incretin analogues include injectable GLP-1, oral GLP-1, and GLP-1/GIP dual-receptor agonists
International markets 2026 Q2	Sales; IQVIA in 2026 April–May monthly data	54.9%	45.1%	Global market, excluding the U.S. and Puerto Rico; scope covers major traditional, oral, injectable, and dual-receptor Incretin products

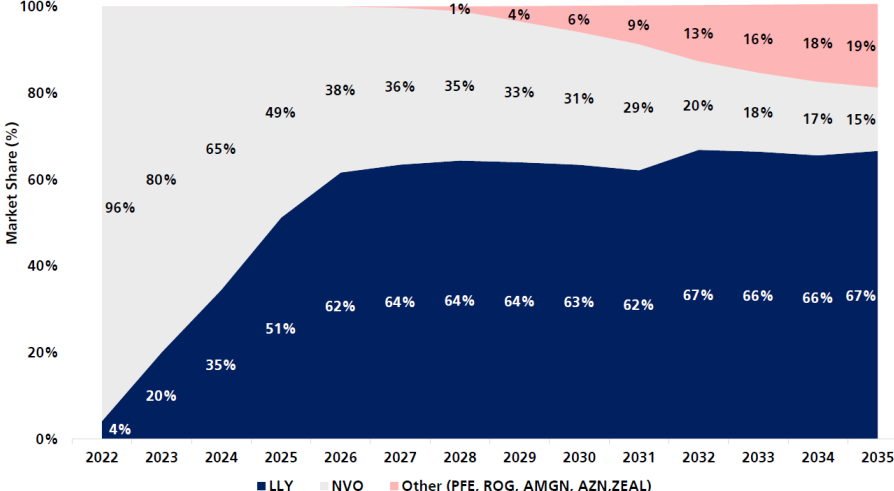
US Incretin Analogs Market



International Incretin Analogs Market



Eli Lilly market share is expected to rise moderately



			Mkt Cap (USD mil)	Price Changes (%)				Last BBG			Sales YoY (%)		EPS YoY (%)		Gross Margin		Net Margin		ROE		P/E		P/B	
				Name	1M	3M	YTD	1YR	Price	Tgt	Px	Upside	2026	2027	2026	2027	2026	2027	2026	2027	2026	2027	2026	2027
LLY US Equity	ELI LILLY & CO	禮來	1,058,283	-8.7	-1.1	4.6	49.0	1,124	1,335	19%	35.5	15.4	51.4	28.5	84.1	84.0	37.0	41.3	82.1	65.7	30.7	23.9	19.9	12.7
NVO US Equity	NOVO NORDISK	諾和諾德	198,960	-6.6	4.1	-12.4	-18.0	45	47	5%	-2.1	1.3	N/A	0.3	80.3	80.4	33.0	31.0	46.7	37.9	13.1	13.1	5.5	4.9

Source: JPM, UBS, LLY, KGI

Lilly vs Novo Nordisk: How Eli Lilly Overtook Novo Nordisk to Establish a Category Lead

A closed-loop playbook: Clinical Efficacy → Scale Capex → Direct-to-Consumer Vials → PBM/Medicare Formulary Access

1. Efficacy attracts patients : dual-receptor GIP/GLP-1 vs single-receptor

- **Target breakthrough:** Novo Nordisk's semaglutide (Semaglutide) acts only on GLP-1 single receptor; whereas Lilly's tirzepatide (Tirzepatide) is **GLP-1/GIP glucose-dependent insulinotropic polypeptide dual-receptor agonist**.
- **Faster, greater weight loss:** Phase 3 head-to-head trials (SURPASS / SURMOUNT series) show that tirzepatide demonstrates an average **20%–25%** weight-loss magnitude and stronger glycaemic efficacy (versus semaglutide's approximately **15%–17%** weight-loss magnitude). Clinically, the direct data of "faster, greater weight loss" have driven many endocrinologists and obesity specialists to select Lilly's product as the preferred new-prescription (NBRx) medication.

2. Manufacturing capacity supports volume: aggressive Capex , helped it emerge first from supply shortages

- GLP-1 drugs' commercialization bottleneck is not demand but sterile auto-injector **filling and sealing (Fill-Finish) capacity**.
- Novo Nordisk early on was hit by severe stockouts because CMO contract manufacturers (e.g. Catalent) had limited capacity;
- By contrast, **Lilly pursued an aggressive build-and-buy strategy, investing >US\$20bn** to expand active pharmaceutical ingredient (API) and sterile fill-finish capacity across Indiana, North Carolina, and Germany, alongside acquiring Nexus Pharmaceuticals.

3. Channel and pricing innovation: LillyDirect and single-dose vial presentation

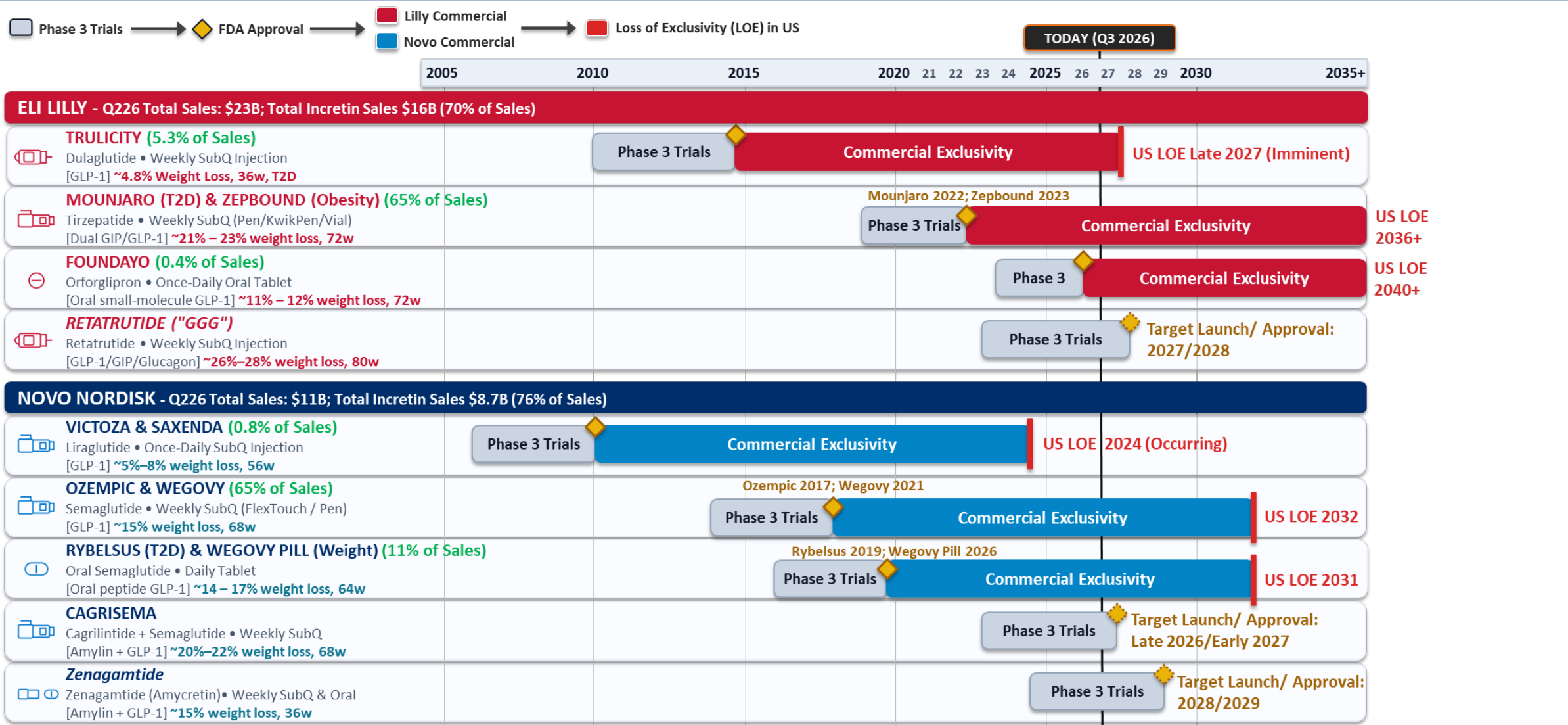
- For cash-pay patients without insurance (Medicare/commercial insurance), **Lilly launched LillyDirect (direct-to-consumer self-pay platform)**, offering single-dose vials priced at US\$399 (2.5mg) and US\$549 (5.0mg), lowering the trial barrier and bypassing pen device bottlenecks.
- The vial presentation not only reduced 50% or more of production-line packaging costs (avoiding the pen-component bottleneck), it also **significantly lowered the barrier to initial patient trial**, converting many self-pay patients previously excluded by high price into stable repeat customers.

4. Payer-locked long tail: PBM formulary negotiation and expansion into comorbid indications

- Lilly demonstrated high commercial agility in formulary negotiations with leading PBMs (CVS Caremark, Express Scripts).
- Label expansions for Zepbound in OSA and cardiovascular disease unlocked early Medicare Part D reimbursement under \$2,000 cap policy, capturing premium regulatory payer incremental reimbursement.

Lilly vs Novo Nordisk: Superior Efficacy Profiles and Extended Patent Exclusivity Horizons

From (Phase 3) to U.S. patent expiry (LOE)



Source: JPM, UBS, KGI, 1 USD = 6.85 DKK.

1. Medicare Reform: Inaugural Implementation of Direct Government Price Negotiation

Biopharma agrees to Maximum Fair Price (MFP) on initial 10 drugs in exchange for tariff exemptions; selective GLP-1 obesity coverage initiated

1. First 10 IRA Negotiated Drugs: Maximum Fair Price (MFP) Formally Effective Jan 1, 2026

- **Covers 10 blockbuster therapies**, including Apixaban (Eliquis), Empagliflozin (**Jardiance**), and Rivaroxaban (Xarelto), with **negotiated price reductions ranging from 38% to 79%**.
- **Practical impact:** This marks the first time in Medicare's 60-year history that the US government directly determines statutory reimbursement prices. Medicare Part D beneficiaries will purchase these drugs directly at negotiated discounts, **projecting ~US\$6bn in first-year Medicare program savings**.

2. Most Favored Nation (MFN) Framework & Tariff Resolution

- **From executive order to voluntary agreement:** Previously, attempts to force U.S. drug prices to anchor to OECD lowest-country prices via MFN executive orders were blocked by the courts. MFN framework negotiations—major drugmakers (such as Pfizer, Eli Lilly, etc.) commit, in specific channels (such as Medicare, Medicaid and DTC direct-to-consumer platforms) to price reductions or transparent discounts, **bringing U.S. effective prices closer to international most-favoured levels**.
- **In exchange for policy waivers:** In return, the U.S. government granted relevant drugmakers **active pharmaceutical ingredient (API) and tariff exemptions on finished-product imports, and expedited regulatory review for selected pipeline items**. This agreement's implementation has largely cleared the regulatory policy overhang that long burdened the pharmaceutical industry.

3. CMS 2026 full rollout of reimbursement for obesity and GLP-1 drugs.

- **A precedent-setting move:** Law previously prohibited Medicare from reimbursing drugs prescribed solely for 'weight loss'. CMS has updated its reimbursement guidance, effective 2026, to formally include (e.g., cardiovascular disease, type 2 diabetes, obstructive sleep apnea) **GLP-1 receptor agonist weight-loss drugs** (e.g., Zepbound, Wegovy) **within Medicare and Medicaid coverage**.
- **Market impact:** The move opens access for tens of millions of elderly and low-income beneficiaries; patients' **average monthly out-of-pocket drug costs fall from over a thousand dollars to tens of dollars**. GLP-1 commercialization is scaling into a new growth phase.

4. Part D out-of-pocket cap (\$2,000 Cap) implemented

- **Out-of-pocket cap:** From 2025/2026 onward, Medicare Part D outpatient prescription drug beneficiaries' annual out-of-pocket spending will be capped at 2,000 USD. (2024 — prior to which a required 5% out-of-pocket Coinsurance, uncapped; Transition phase 2024, the effective out-of-pocket cap was implicitly set at approximately \$3,200 – \$3,300 USD)
- **Structural impact:** coupled with 2026 effective MFP negotiated prices, materially reducing drug cost burden for elderly patients with serious and chronic illnesses, prompting PBMs to readjust formularies, removing high-cost drugs that lack clinical advantage.

1. Medicare reform: Assessing Eli Lilly's Exposure to Price Negotiations

A mature co-promoted asset absorbs a 66% MFP cut, while core metabolic growth engines gain broad coverage

1. Mature/Co-Promoted Franchises (Primary Headwinds)

- **Jardiance (Empagliflozin - T2D / Heart Failure):** Co-promoted with Boehringer Ingelheim; subject to a 66% MFP reduction effective 1 Jan, 2026 under initial IRA negotiations.
- **Trulicity (Dulaglutide - 1st-Gen GLP-1):** Faces imminent patent expiry (US LOE late 2027) and potential subsequent negotiation exposure; revenue erosion is actively mitigated by patient migration to Mounjaro.

2. Core Metabolic Growth Drivers (Primary Beneficiaries)

- **Zepbound (Tirzepatide - Obesity):** Gains formal Medicare and Medicaid reimbursement in 2026 under updated CMS comorbidity guidelines, unlocking substantial covered volume.
- **Mounjaro (Tirzepatide - T2D):** Secures predictable Part D formulary reimbursement with net channel pricing protected under MFN framework agreements.
- **Orforglipron (Foundayo - Oral Small-Molecule GLP-1):** Following its April 2026 launch, leverages established MFN pricing and access frameworks, pairing with LillyDirect to accelerate self-pay and commercial uptake.

3. Other major pipeline (Beneficiaries)

- **Donanemab (Alzheimer's Disease):** Benefits from clear CMS coverage determinations for amyloid-targeting monoclonal antibodies under Medicare Part B.

1. Medicare reform: Net positive for Eli Lilly

Price-for-volume + Removal of policy uncertainty > Jardiance losses from price cuts

1. Unlocks an Addressable Patient Pool of ~25 Million Covered Lives, realizing significant price-for-volume

- **Breaks policy taboo:** Previously, federal law prohibited Medicare from covering purely weight-loss drugs. Following CMS policy revisions, therapies accompanied by cardiovascular or metabolic comorbidities are now fully eligible for Medicare Part D coverage.
- **Unleashes huge demand:** This directly opens access to approximately 25 million additional beneficiaries across Medicare and Medicaid, realizing massive price-for-volume growth.
- **Commercial payor follow-through:** Medicare has set pricing at approximately US\$245/month (far below the original near-\$1,000 monthly list price), meeting or even exceeding market expectations. With this national benchmark established, commercial payors will also accelerate reimbursement, fully unlocking commercial volume beyond self-pay.

2. De-risking of Regulatory Policy Overhang Prompts Multiple Re-rating

- **Eliminates tariff and punitive price-cut risk:** Eli Lilly, by reaching MFN-related agreements and committing to U.S. domestic manufacturing, obtained tariff exemptions, thereby effectively removing DC (Washington) policy risk.
- **Improved revenue visibility:** Investors' main prior concern was that the government would relentlessly push down obesity-drug prices. With a clear pricing framework now in place, Eli Lilly's 2026–2030 revenue growth trajectory is visible (the market forecasts its PEG at only 1.7x, valuing it well below mega-cap tech peers at 2.5x).

3. Strong Hedge Against Price-cut Losses To Legacy Drug (Jardiance)

- **Mitigating mature asset headwinds:** Although Jardiance in 2026 is facing 66% Medicare price-reduction pressure, the drug is in the mid-to-late lifecycle stage, and price-cut losses are shared between Eli Lilly and Boehringer Ingelheim.
- **Volume outweighing the shortfall:** Zepbound, Mounjaro, and Orforglipron's incremental volumes will far outweigh the Jardiance price-reduction shortfall. For example, Orforglipron alone, as a single oral drug, is projected to achieve 2026 sales of US\$1.5–1.6bn, scaling to an estimated long-term peak of US\$25bn.

2. Eli Lilly GLP-1 Product Portfolio Comparison:

Retatrutide as the Next Triple-Receptor Agonist Focus

	Trulicity (Dulaglutide) 1st-Gen GLP-1 (Mature Anchor)	Zepbound/Mounjaro (Tirzepatide) 2nd-Gen Incretin (Current Flagship)	Foundayo (Orforglipron) Oral Small-Molecule GLP-1	Retatrutide (GGG) 3rd-Gen Triple Incretin Agonist
Molecular type and mechanism	Peptide-fusion protein, single GLP-1 receptor agonist	Synthetic peptide, dual GIP / GLP-1 receptor agonist	Non-peptide small molecule, oral GLP-1 receptor agonist	Synthetic peptide, triple GIP / GLP-1 / Glucagon agonist
Market Launch	2014	2022 (Mounjaro) / Late 2023 (Zepbound)	April 2026	2027–2028E (Phase 3 ongoing)
LOE Timing (Patent Expiry)	~2027 - 2029 (imminent patent expiry)	~2036 (Core patent moat & revenue anchor)	~2040+ (New small-molecule composition patent)	~2040+ (New multi-receptor composition patent))
Route of Administration	Once-weekly subcutaneous injection (requires cold-chain storage)	Once-weekly subcutaneous injection (cold chain; DTC single-dose vials available)	Once-daily oral tablet (no fasting or water restrictions)	Once-weekly subcutaneous injection (requires cold-chain storage)
Current Monthly Drug Cost	USD 970 - 1,000 WAC list price	USD 1,060 WAC list price; LillyDirect single-dose vials US\$399–\$549	~USD 558 WAC list price; LillyDirect self-pay ~USD 149–\$399	Not yet launched (Projected Flagship Tier USD 1,100–\$1,300)
Mean Weight-Loss Efficacy	3%–5% (Modest reduction; primary T2D focus)	20% – 22.5% (SURMOUNT high-dose)	14% - 15% (36 weeks)	24%+ (48 weeks, current industry efficacy ceiling)
Glycemic Efficacy (HbA1c)	-1.2% to -1.5%	-2.0% to -2.5% (Robust glycemic control)	-1.3% to -1.8%	-1.4% to -2.1% (T2D weight loss also reaches 20%+)
Clinical Advantages & Differentiation	Established glycemic control with mature cardiovascular outcomes (CVOT) data	Dual-target mechanism establishes clinical superiority over Semaglutide; first to secure OSA label with broad CV pipeline expansion	Eliminates needle phobia; superior patient adherence; zero cold-chain dependency	Glucagon co-agonism elevates basal metabolic rate and clears hepatic fat
Primary Target Indications	Type 2 Diabetes (T2D); cardiovascular risk reduction	Type 2 Diabetes, Obesity / Overweight, OSA, heart failure	Mild-to-moderate obesity, T2D, long-term post-loss weight maintenance	Severe obesity, MASH / liver fibrosis, complex metabolic syndrome
Supply Chain & Manufacturing Costs	Biologic peptide; auto-injector pen constrained; capacity expansion limited	Complex peptide synthesis; fill-finish constrained; backed by >US\$20bn in capex expansion	Standard small-molecule chemical synthesis; ultra-low COGS; zero device or cold-chain constraints; highly scalable	Complex multi-peptide synthesis; auto-injector pen required; positioned for premium high-margin tier

2. Next growth engine/share-price catalyst: Retatrutide (GLP-1 3.0, GGG)

Four Core Strategic Pillars Underpinning Lilly's Long-Term Leadership

Commercial Strategy: Seamless Product Portfolio Migration

- **Tirzepatide (Mounjaro / Zepbound)** represents Lilly's primary cash generator (**65% of 2026E total revenue**), having overtaken Semaglutide to capture global volume leadership. However, long-term expansion faces high peptide synthesis costs and auto-injector fill-finish constraints.
- **Lilly is simultaneously advancing a two-pronged portfolio upgrade**
 - **Orforglipron** (Oral Small Molecule): Ultra-low COGS and oral convenience penetrate primary care, emerging markets, and self-pay DTC channels, maximizing overall volume share.
 - **Retatrutide 'GGG'** (Triple Agonist): Sets the maximum efficacy ceiling at premium margins, defending market share and driving seamless patient migration ahead of Trulicity's late-2027 patent expiry.

1. Redefining the Clinical Efficacy Ceiling

- **Current Benchmarks:** Baseline Tirzepatide achieves ~13%–16% weight reduction in T2D cohorts (and ~21% in obesity).
- **Setting a New Standard:** As a triple GIP/GLP-1/Glucagon agonist, Retatrutide achieves **20%–21% weight loss in T2D** and up to **24%+ in obesity**, resetting the efficacy ceiling for non-surgical therapy.

2. Post-2030 Franchise Defense & Migration

- **Patent Cliff Defense:** As legacy incretin therapies face post-2030 patent expiries (LOE) and generic erosion, Lilly is establishing a high-barrier, long-dated patent moat.
- **Next-Gen Upgrades:** Retatrutide (GLP-1 3.0 triple agonist) and Orforglipron (oral small molecule) serve as Lilly's core platforms to migrate patients to higher-efficacy, better-tolerated therapies.

3. Hepatic & Metabolic Benefits via Glucagon

- **Metabolic Activation:** Glucagon co-agonism elevates basal energy expenditure and stimulates direct hepatic lipid beta-oxidation.
- **Organ Protection:** Confers unmatched clinical benefits in MASH (steatohepatitis), severe hypertriglyceridemia, and metabolic syndrome that legacy mono- or dual-target agents cannot match.

4. Commercial Dosing Flexibility & Safety Latitude

- **Low-Dose Profile:** At low doses (e.g., 4mg), Retatrutide delivers ~19% weight loss with minimal gastrointestinal adverse events (nausea/vomiting).
- **Prescribing Latitude:** Higher doses allow clinicians to push efficacy to the maximum threshold, offering an exceptionally wide therapeutic window..

2. Next-Generation Growth Engine: Retatrutide (GLP-1 3.0, "GGG")

Phase 3 TRIUMPH Program Execution: Global NDA Filings Targeted for 2026–2027

Obesity Registration Cohort (TRIUMPH-1):

Published Phase 3 data confirm up to **24%+ mean weight loss** at high doses; the 4mg low-dose regimen delivers ****19% weight reduction**** with excellent GI tolerability.

Type 2 Diabetes Registration Cohort (TRIUMPH T2D):

Phase 3 data demonstrate **20%–21% weight loss** in T2D patients and a **1.4%–1.6% HbA1c reduction**, bringing most patients below the ADA 7.0% clinical target.

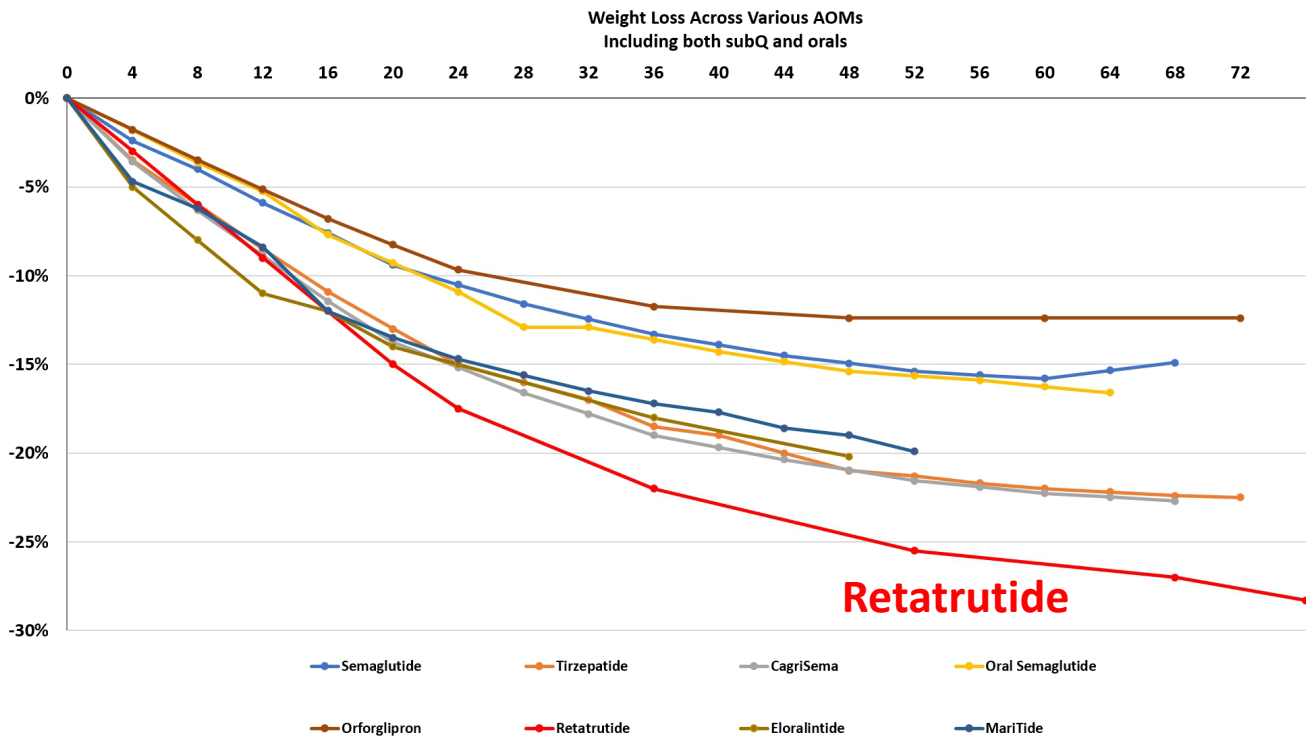
Cardiovascular & Metabolic Endpoints (TRIUMPH-3):

In established CVD cohorts, demonstrated a favorable trend in MACE-5 reduction (HR 0.82) alongside significant improvements in blood pressure, triglycerides, and glycemic control.

Cardiovascular Outcomes Trial (TRIUMPH-Outcomes):

Large-scale hard-endpoint CVOT evaluating long-term cardiovascular risk reduction; primary trial completion targeted for **2029**.

Retatrutide: Approaching ~30% Weight Loss at 72 Weeks



3. Eli Lilly - Strong Financial Performance + High Visibility

Name			Mkt Cap (USD mil)	Price Changes (%)				Last Price	BBG Tgt Px	Upside	Sales YoY (%)		EPS YoY (%)		Gross Margin		Net Margin		ROE		P/E		P/B	
				1M	3M	YTD	1YR				2026	2027	2026	2027	2026	2027	2026	2027	2026	2027	2026	2027	2026	2027
生物科學與診斷 & Diagnostics																								
TMO US Equity	THERMO FISHER SCIENTIFIC INC	賽默飛世爾	223,952	1.0	25.7	4.5	27.1	606	652	8%	7.4	5.2	9.8	9.6	41.9	42.3	19.5	20.2	16.6	16.7	24.1	22.0	4.0	3.6
DHR US Equity	DANAHER CORP	丹納赫集團	144,007	-2.2	11.6	-10.5	6.4	205	226	10%	6.8	8.0	9.1	9.3	59.0	59.6	23.0	23.2	11.4	11.7	24.1	22.0	2.7	2.5
2359 HK Equity	WUXI APPTCCO LTD-H	無錫藥明康德	69,899	-3.5	58.6	93.5	65.9	191	224	18%	32.1	21.1	16.6	17.3	53.1	53.0	38.1	36.9	26.6	25.8	20.8	17.8	5.1	4.2
A US Equity	AGILENT TECHNOLOGIES INC	安捷倫	40,809	-2.7	10.0	6.4	16.6	145	176	22%	8.0	6.5	10.9	8.8	55.0	55.1	23.4	23.8	23.1	21.5	23.3	21.4	5.1	4.4
2269 HK Equity	WUXI BIOLOGICS CAYMAN INC	藥明生物	25,175	3.0	59.9	51.1	26.3	48	58	22%	17.7	19.8	16.8	20.4	46.1	46.9	25.1	25.4	11.2	12.2	26.2	21.7	3.0	2.7
TEM US Equity	TEMPUS AI INC-CL A	Tempus AI	11,057	11.3	23.8	3.8	-21.6	61	66	8%	25.5	23.3	62.0	122.8	65.2	65.6	-2.6	-0.2	-5.5	0.4	N/A	1,156	24.4	22.9
Simple Average			85,817	1.2	31.6	24.8	20.1			15%	16.3	14.0	20.9	31.4	53.4	53.7	21.1	21.6	13.9	14.7	23.7	210.2	7.4	6.7
Market Cap Weighted Average				-0.5	26.6	14.8	24.7			12%	11.5	9.3	12.1	13.5	50.0	50.3	23.1	23.4	16.3	16.4	23.2	45.7	4.3	3.8
製藥與生物科技 & Biotechnology																								
LLY US Equity	ELI LILLY & CO	禮來	1,058,283	-8.7	-1.1	4.6	49.0	1,124	1,335	19%	35.5	15.4	51.4	28.5	84.1	84.0	37.0	41.3	82.1	65.7	30.7	23.9	19.9	12.7
JNJ US Equity	JOHNSON & JOHNSON	嬌生	643,636	2.0	12.0	29.1	51.9	267	282	6%	7.5	7.3	7.1	10.0	73.0	73.2	27.9	28.4	32.8	33.2	23.1	21.0	7.3	6.4
ABBV US Equity	ABBVIE INC	艾伯維	443,387	1.2	11.5	9.8	18.6	251	280	12%	10.6	8.9	40.4	15.8	84.3	84.6	36.9	39.2	-64.0	-1,625	17.9	15.4	N/A	N/A
MRK US Equity	MERCK & CO. INC.	默克藥廠	363,982	12.7	23.9	40.2	75.6	148	151	2%	3.3	4.8	-69.4	247.7	81.1	82.3	10.1	33.4	13.9	42.8	53.7	15.4	7.5	6.0
RHHBY US Equity	ROCHE HOLDINGS LTD-SPONS ADR	羅氏控股	346,996	-7.1	5.9	3.5	27.6	53	61	13%	1.7	5.0	N/A	7.3	75.6	76.0	25.6	26.4	42.3	38.0	17.0	15.8	6.8	5.8
NVS US Equity	NOVARTIS AG-SPONSORED ADR	諾華	279,747	-12.3	-7.2	-0.3	8.6	137	159	16%	4.4	6.2	N/A	10.6	80.6	80.4	29.7	30.5	35.4	36.5	15.4	13.9	5.6	5.1
AZN LN Equity	ASTRAZENECA PLC	阿斯捷利康	244,952	-2.8	-13.5	-15.5	-2.2	11,650	15,655	34%	7.8	6.3	12.3	11.2	82.3	82.3	25.2	25.9	26.6	26.5	15.4	13.8	4.5	3.9
NVO US Equity	NOVO NORDISK	諾和諾德	198,960	-6.6	4.1	-12.4	-18.0	45	47	5%	-2.1	1.3	N/A	0.3	80.3	80.4	33.0	31.0	46.7	37.9	13.1	13.1	5.5	4.9
PFE US Equity	PFIZER INC	輝瑞	158,337	2.7	8.5	11.6	13.1	28	29	4%	-0.4	-3.8	-7.5	-2.6	75.1	75.7	27.3	27.5	18.1	18.3	9.3	9.6	1.8	1.7
VRTX US Equity	VERTEX PHARMACEUTICALS INC	福泰製藥	132,084	-0.5	19.6	14.9	34.1	521	573	10%	10.2	10.4	2.9	11.3	86.1	87.3	36.6	36.7	22.6	23.1	27.5	24.7	5.9	4.9
REGN US Equity	REGENERON PHARMACEUTICALS	Regeneron Pharm	83,152	-0.0	34.2	4.6	45.3	808	857	6%	18.5	9.5	22.1	11.9	84.7	85.0	34.7	35.5	17.0	15.7	14.9	13.3	2.4	2.2
1276 HK Equity	JIANGSU HENGRUI PHARMACEUT-H	江蘇恒瑞醫藥	42,553	-23.4	-17.6	-37.7	-48.2	44	75	70%	7.9	14.2	15.0	12.0	86.4	86.4	26.7	26.1	13.9	13.5	27.8	24.8	3.7	3.3
SDZ SW Equity	SANDOZ GROUP AG	山德士	36,234	-7.7	1.1	15.4	38.4	67	75	13%	9.0	5.0	11.6	11.8	49.2	50.2	14.7	15.7	14.3	16.5	20.3	18.1	3.6	3.1
Simple Average			310,177	-3.9	6.3	5.2	22.6			16%	8.8	6.9	8.6	28.9	78.7	79.1	28.1	30.6	-21.1	-96.7	22.0	17.1	6.2	5.0
Market Cap Weighted Average				-2.9	6.0	10.1	34.4			13%	13.6	8.5	14.1	36.0	80.2	80.5	30.0	33.6	-30.2	-140.9	24.7	18.4	9.0	6.6
醫療器械與醫療科技																								
ABT US Equity	ABBOTT LABORATORIES	亞培	182,088	-3.1	18.0	-16.0	-18.7	105	121	15%	13.5	8.7	7.2	9.8	57.8	58.1	19.2	19.3	18.5	19.9	19.1	17.4	3.6	3.4
ISRG US Equity	INTUITIVE SURGICAL INC	直覺外科公司	124,792	-10.2	-14.3	-37.6	-21.5	353	476	35%	16.8	12.7	20.6	10.8	68.4	68.5	32.8	32.5	19.0	18.5	32.8	29.6	6.1	5.1
MDT US Equity	MEDTRONIC PLC	美敦力公司	117,540	2.8	14.5	-4.3	-0.5	92	104	13%	8.4	7.3	0.7	8.1	65.4	65.0	19.7	19.7	14.6	15.2	16.6	15.4	2.5	2.3
SYK US Equity	STRYKER CORP	史賽克公司	105,632	-20.4	-10.8	-21.6	-28.1	275	378	37%	8.6	8.4	10.2	11.5	65.2	65.5	21.3	21.9	22.2	21.1	18.3	16.4	4.1	3.7
Simple Average			132,513	-7.7	1.9	-19.9	-17.2			25%	11.8	9.3	9.7	10.1	64.2	64.3	23.3	23.4	18.6	18.7	21.7	19.7	4.1	3.6
Market Cap Weighted Average				-6.9	3.9	-19.6	-17.2			24%	12.2	9.3	9.5	10.0	63.4	63.6	22.9	23.0	18.5	18.8	21.6	19.6	4.0	3.6
醫療IT & Digital Health																								
VEEV US Equity	VEEVA SYSTEMS INC-CLASS A	衛視公司	42,226	11.1	59.3	16.8	-5.0	261	297	14%	16.3	15.4	22.7	14.0	78.0	76.8	42.1	41.4	19.4	18.0	32.8	28.2	6.0	5.4
HIMS US Equity	HIMS & HERS HEALTH INC	他和她的健康公司	6,509	-12.2	0.4	-14.1	-41.6	28	32	15%	36.7	25.0	-92.0	9,688	65.0	64.7	3.2	5.6	-14.5	25.0	3,488	35.6	4.2	3.5
Simple Average			24,368	-0.5	29.8	1.4	-23.3			15%	26.5	20.2	-34.6	4,851	71.5	70.8	22.6	23.5	2.5	21.5	1,760	31.9	5.1	4.5
Market Cap Weighted Average				8.0	51.4	12.7	-9.9			14%	19.1	16.7	7.4	1,306	76.2	75.2	36.9	36.6	14.9	18.9	494.3	29.2	5.7	5.2
醫療服務機構 Services & Providers																								
HCA US Equity	HCA HEALTHCARE INC	醫療保健	91,327	1.9	13.0	-9.6	7.0	422	453	7%	3.9	3.8	4.5	8.7	N/A	N/A	8.3	8.1	-92.9	-72.3	14.3	13.2	N/A	N/A
ALCSW Equity	ALCON INC	愛爾康公司	33,634	-6.5	1.6	-13.8	-13.7	55	73	33%	7.1	6.0	15.2	14.1	63.5	63.3	15.5	16.3	5.6	7.2	19.0	16.7	1.4	1.4
Simple Average			62,480	-2.3	7.3	-11.7	-3.4			20%	5.5	4.9	9.8	11.4	63.5	63.3	11.9	12.2	-43.7	-32.6	16.7	14.9	1.4	1.4
Market Cap Weighted Average				-0.4	9.9	-10.8	1.4			14%	4.8	4.4	7.4	10.2	17.1	17.0	10.2	10.3	-66.4	-50.9	15.6	14.1	0.4	0.4
醫療保險與支付方																								
UNH US Equity	UNITEDHEALTH GROUP INC	聯合健康	352,809	-3.8	-3.5	19.1	13.3	393	481	22%	-0.4	3.1	21.5	13.7	19.8	19.6	4.0	4.4	17.3	19.0	19.8	17.4	3.5	3.2
1299 HK Equity	AIA GROUP LTD	友邦保險	99,359	1.1	7.2	-5.8	-1.1	75	103	36%	10.6	9.6	14.4	10.1	N/A	54.0	33.2	33.4	17.7	18.1	12.4	11.3	2.2	2.0
ELV US Equity	ELEVANCE HEALTH INC	健安施	86,075	-0.2	-1.9	13.2	29.4	397	446	12%	-0.5	2.3	-10.3	8.7	19.1	19.9	3.0	3.1	11.6	12.8	14.6	13.4	1.9	1.7
CI US Equity	THE CIGNA GROUP	信諾集團	73,504	-0.1	-6.0	1.1	-8.0	278	339	22%	4.7	4.4	2.2	9.8	9.2	9.2	2.8	2.8	17.5	17.6	9.1	8.3	1.7	1.5
Simple Average			152,937	-0.8	-1.1	6.9	8.4			23%	3.6	4.8	6.9	10.6	16.0	25.7	10.8	11.0	16.0	16.9	14.0	12.6	2.3	2.1
Market Cap Weighted Average				-2.1	-1.9	12.1	10.7			23%	2.0	4.2	13.5	11.9	15.2	24.0	8.5	8.8	16.5	17.8	16.6	14.8	2.8	2.6
Health Care - Simple Average			189,119	-2.7	11.2	4.6	10.5			18%	10.9	9.1	8.1	334.5	63.9	63.8	22.5	23.7	-4.3	-33.8	136.7	55.1	5.4	4.6
Health Care - Market Cap Weighted Average				-2.8	7.2	7.6	25.3			15%	12.0	8.2	13.2	39.1	67.9	69.0	26.1	28.7	-17.2	-92.8	27.2	20.5	7.3	5.5

Among global pharmaceutical leaders

- Fastest revenue and earnings growth
- Sector-Dominant Margins
- Highest ROE
- Compelling PEG Ratio

3. Strong Financial Performance + High Visibility: Fastest Top/Bottom-Line Growth Among Biopharma Majors

禮來 (LLY) in USD million	2022	2023	2024	2025	2026F	2027F	2028F	2029F	2030F	25-30 CAGR
Revenue	28,541	34,124	45,043	65,179	89,832	101,404	112,013	120,856	127,656	14%
YoY(%)	100%	20%	32%	45%	38%	13%	10%	8%	6%	
Diabetes & Metabolic	14,465	19,667	29,521	48,222	71,143	80,808	89,645	96,939	103,384	16%
YoY(%)	51%	58%	66%	74%	79%	80%	80%	80%	81%	
Immunology	3,345	3,798	4,393	5,248	5,969	6,598	7,190	7,723	6,975	6%
Neuroscience	1,546	2,879	1,474	1,390	1,794	2,391	3,088	3,795	4,477	26%
Oncology	5,666	6,658	8,753	9,377	10,091	10,854	11,407	11,745	12,194	5%
Other	3,520	1,122	903	942	834	753	683	654	626	-8%
Gross Profit	22,486	27,548	37,178	54,615	75,010	84,470	93,979	102,305	108,125	
YoY(%)	2.7%	22.5%	35.0%	46.9%	37.3%	12.6%	11.3%	8.9%	5.7%	
Gross Margin (%)	78.8%	80.7%	82.5%	83.8%	83.5%	83.3%	83.9%	84.7%	84.7%	
Operating expenses	(14,540)	(20,516)	(22,865)	(27,342)	(32,621)	(29,898)	(31,447)	(33,078)	(34,796)	
R&D	(7,191)	(9,313)	(10,991)	(13,338)	(16,058)	(16,299)	(17,033)	(17,799)	(18,600)	
% of Revenue	25.2%	27.3%	24.4%	20.5%	17.9%	16.1%	15.2%	14.7%	14.6%	
Operating Income	7,946	7,031	14,313	27,273	42,389	54,572	62,532	69,226	73,329	
YoY(%)	-5.9%	-11.5%	103.6%	90.5%	55.4%	28.7%	14.6%	10.7%	5.9%	
Operating Margin (%)	27.8%	20.6%	31.8%	41.8%	50.9%	53.8%	55.8%	57.3%	57.4%	
Cash conversion	89.2%	60.3%	61.6%	61.6%	108.9%	84.6%	86.7%	88.1%	88.4%	
Net Income (Non GAAP)	7,186	5,712	11,747	21,768	33,430	44,558	51,819	57,582	61,112	23%
YoY(%)	-3.2%	-20.5%	105.6%	85.3%	53.6%	33.3%	16.3%	11.1%	6.1%	
Net Income Margin (%)	25.2%	16.7%	26.1%	33.4%	37.2%	43.9%	46.3%	47.6%	47.9%	
Dividend Payout ratio (%)	56.6%	77.7%	44.2%	26.1%	14.3%	12.6%	11.4%	10.7%	10.5%	

Key forecast risks:

Revenue Concentration

- Tirzepatide (Mounjaro / Zepbound) contributed 56% of 2025 revenue.
- As baseline growth normalizes, sustaining double-digit momentum relies on execution in oral Orforglipron and triple-agonist Retatrutide.
- Key competitor (Novo Nordisk) Weight-loss drug patents expiring overseas, facing low-priced generic competition

Oral Foundayo (Obesity)

- Oral drug conversion rate (most currently marketed are products predominantly injectable due to superior efficacy)
- Oral market share (Foundayo has fewer dosing restrictions but slightly lower efficacy versus competitors, making conversion rate critical)
- 2026–2030 revenue CAGR of 91%, contributing 2030 total revenue of 8.4%

Triple-receptor Retatrutide (Obesity)

- Although the pivotal Phase 3 trials met endpoints, Biologics License Application (BLA) submission and the FDA review timetable will be critical.
- Market expects earliest 2027 Q4 for launch.
- 2028–2030 revenue CAGR of 83%, contributing 2030 total revenue of 4.4%

3. Strong Financial Performance + High Visibility: Healthy Cash flows, Transitioning to Substantial Net Cash

禮來 (LLY US Stock)

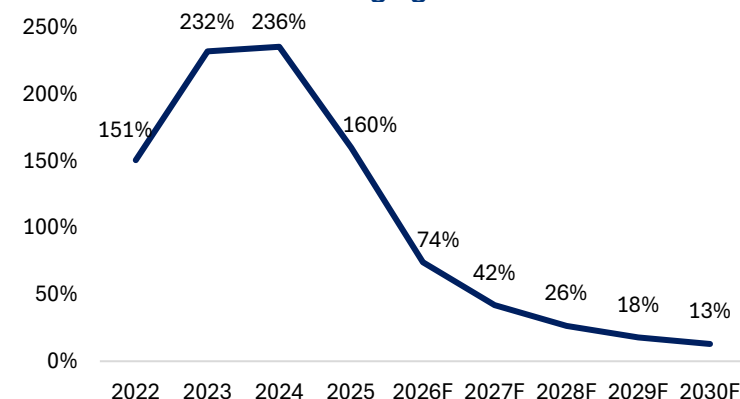
Balance Sheet (USD Millions)		2022	2023	2024	2025	2026F	2027F	2028F	2029F	2030F
Key Metric	Net Debt	14,172	22,407	30,376	35,235	5,363	(23,897)	(62,640)	(108,865)	(160,130)
Assets (Key Element)	Cash & Equivalents	2,067	2,819	3,268	7,268	35,847	62,591	98,078	141,226	190,359
	Inventories	4,310	5,773	7,589	13,744	9,264	10,584	11,271	11,595	12,207
	Accounts receivable	6,896	9,091	11,006	17,760	21,389	24,144	26,670	28,775	30,394
	Total assets	49,490	64,006	78,715	112,476	148,575	185,700	227,433	274,590	326,519
Liabilities (Key Element)	Short term debt	1,501	6,905	5,117	1,635	2,516	3,256	3,077	2,132	-
	Long term debt	14,738	18,321	28,527	40,868	38,694	35,438	32,361	30,229	30,229
	Accounts payable	1,931	2,599	3,229	5,379	7,726	8,721	9,633	10,394	10,978
	Total liabilities	38,714	53,143	64,443	85,941	92,983	93,835	93,666	93,162	93,009
Equity (Key Element)	Retained earnings	10,043	10,312	13,545	24,470	57,878	98,481	145,689	198,631	254,970
	Additional paid-in capital	6,921	7,250	7,439	7,346	2,994	(1,336)	(6,641)	(11,923)	(16,180)
	Total Equity	10,775	10,864	14,272	26,535	55,592	91,865	133,767	181,428	233,510
Cash Flow Statement (USD Millions)		2022	2023	2024	2025	2026F	2027F	2028F	2029F	2030F
Operating CF (Key Element)	Net income	6,245	5,240	10,590	20,640	38,992	46,433	53,291	59,292	62,977
	Depreciation and amortization	1,523	1,527	1,767	1,997	2,583	3,120	3,399	3,401	3,322
	Accounts payable and other liabilities	1,332	4,274	2,609	10,187	8,335	3,367	3,087	2,573	1,979
	Net cash from operations	7,084	4,240	8,818	16,813	49,438	46,174	54,186	60,992	64,817
Investing CF (Key Element)	PPE	(1,854)	(3,448)	(5,058)	(7,841)	(8,983)	(6,084)	(3,360)	(2,417)	(1,915)
	Purchases of in-process R&D	(630)	(3,945)	(3,346)	(3,008)	-	-	-	-	-
	Net cash from investing activities	(3,262)	(7,153)	(9,302)	(10,972)	(8,983)	(6,084)	(3,360)	(2,417)	(1,915)
Financing CF (Key Element)	Dividend paid	(3,536)	(4,069)	(4,680)	(5,384)	(5,583)	(5,830)	(6,083)	(6,350)	(6,638)
	Repayments of long-term debt	(1,560)	-	(664)	(778)	(1,293)	(2,516)	(3,256)	(3,077)	(2,132)
	Purchases of common stock	(1,500)	(750)	(2,500)	(4,108)	(5,000)	(5,000)	(6,000)	(6,000)	(5,000)
	Proceeds from issuance of long-term debt	-	3,959	11,417	13,167	-	-	-	-	-
	Net cash from financing activities	(5,407)	3,496	1,230	(2,213)	(11,876)	(13,346)	(15,339)	(15,427)	(13,770)
Cash and cash equivalents at end of year		2,032	2,783	3,233	7,268	35,847	62,591	98,078	141,226	190,359

Eli Lilly balance sheet

- Debt profile is predominantly long-term; the company has sufficient cash to cover short-term liabilities
- Expected in 2027 to become a net-cash company

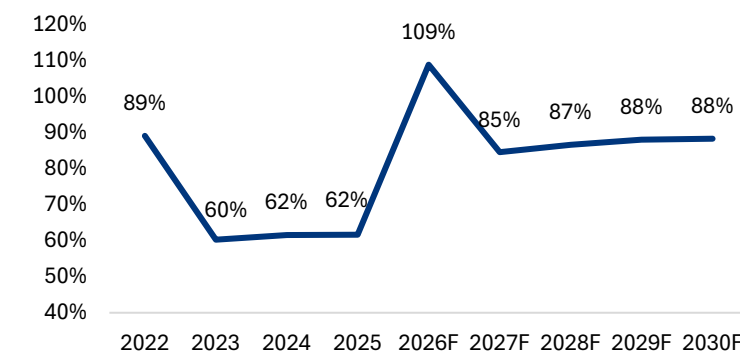
Total Debt/Equity Ratio:

- Monetization of blockbuster incretins drives rapid balance sheet de-leveraging.



Cash Conversion (CFO/Operating income)

- Strong manufacturing margins drive rapid expansion in operating cash conversion.



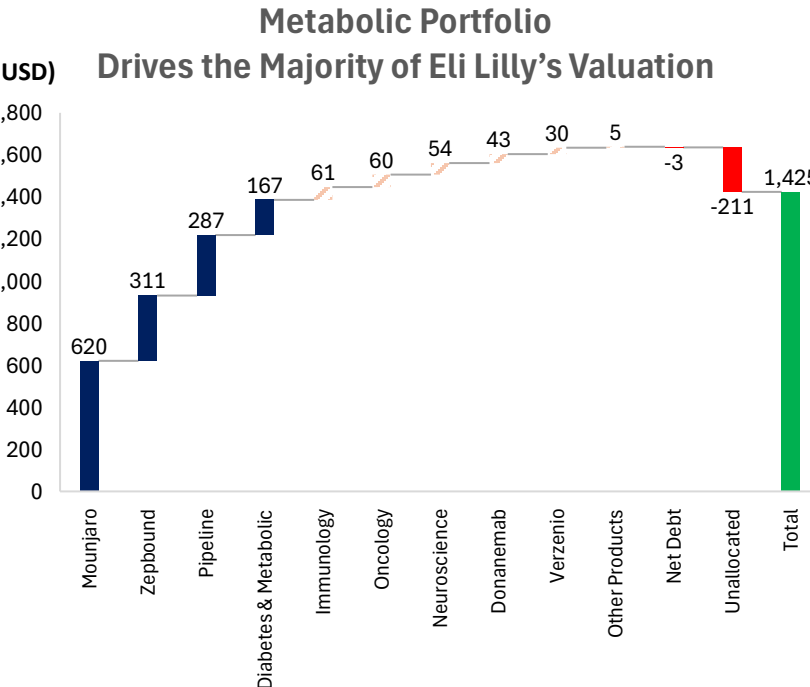
3. Valuation Remains Attractive Relative to Global Healthcare and AI

DCF and P/E

	Fair Value	Valuation Methodology			Fair Value Implied P/E Multiple			
	HK\$/Share	Valuation method	Benchmark Multiple (2026E)	Rationale	2027E	2028E	2029E	2030E
Analyst average	1,332	DCF	35.7x	1. Key drugs have no patent-cliff risk before 2036, providing cash-flow stability and predictability and suitable for discounted cash flow (DCF) valuation 2. 2026-2030 earnings CAGR is 15.7%,PEG at 1.9, vs peers NVO(2.0) and vs AI leaders' average (2.4), leaving room for upside	~26x	~23x	~20x	~19x
		&						
		P/E						

Sell-side institutions		Target price	Scenario analysis	2027E	
				Revenue (million USD)	Non GAAP - EPS (USD)
Citi		1,600	Bull Case (HK\$1,600/shr) Base Case (HK\$1,332/shr) Bear Case (HK\$850/shr) 2025 status	120,062	59.2
DBS Bank		1,550			
Jefferies		1,440			
UBS		1,425			
JP Morgan		1,400	Implied CAGR in Revenue (2025 - 2027)	Revenue	EPS
Goldman Sachs		1,367			
Consensus average		1,332			
Wells Fargo		1,330			
China Merchants Securities		1,252			
Morningstar (Sell)		980	Bull Case (HK\$1,600/shr)	36%	56%
HSBC (Sell)		850	Base Case (HK\$1,332/shr)	25%	44%
			Bear Case (HK\$850/shr)	-1%	14%
Buy	Hold	Sell			
29	5	1			

*Margin improvement drives earnings growth above revenue growth



*Blue segments represent weight-loss drugs; chart data sourced from UBS

Key Investment Risks

Commercial Competition, Pricing Pressure, Pipeline Execution, Patient Adherence

1. Core Franchise Deceleration & Competitive Risk

- GLP-1 receptor agonists (Mounjaro/Zepbound) growth could slow and face peer competition.
- In the near term, unauthorized compounded GLP-1 formulations distributed via telehealth channels capture unauthorized volume; post-2031, generic market entry poses long-term price-compression risk.

2. Drug Pricing Pressure & Policy / Regulatory Risk

- PBM consolidation and vertical integration with healthcare payors weigh on prices.
- Regulatory uncertainty surrounding Inflation Reduction Act (IRA) drug-price negotiations and mandatory rebate restructuring maintains long-term policy overhang.

3. R&D Pipeline & Clinical Attrition Risk

- Lilly's premium valuation is heavily anchored in next-generation incretin pipelines (Orforglipron, Retatrutide); clinical trial setbacks or regulatory delays would materially compress terminal valuation multiples.

4. Margin compression risk

- Deceleration in high-margin incretin sales, mandatory statutory price cuts, or elevated R&D trial expenditures could compress operating margins.

5. Patient Adherence Challenges & Adverse Event Profile

- Elevated 1-year real-world discontinuation rates (~65% in non-diabetic obesity, ~45% in T2D) combined with rapid post-cessation weight regain present commercial retention headwinds.
- Next-generation multi-agonists at higher doses may trigger increased gastrointestinal events (nausea/vomiting) and cardiovascular shifts, such as elevated resting heart rate

Appendix: USD400bn Patent Cliff/LOE Over the Next 8 Years

Pfizer (PFE), Merck (MRK), Bristol Myers Squibb (BMY), and Big Pharma peers must deploy M&A capital to replenish pipeline voids.

What Is Loss of Exclusivity (LOE)?

- **Definition:** Expiration of statutory patent protection or regulatory market exclusivity, allowing third-party manufacturers to legally market generic small molecules or biosimilar biologics.

Precedent LOE Case Studies:

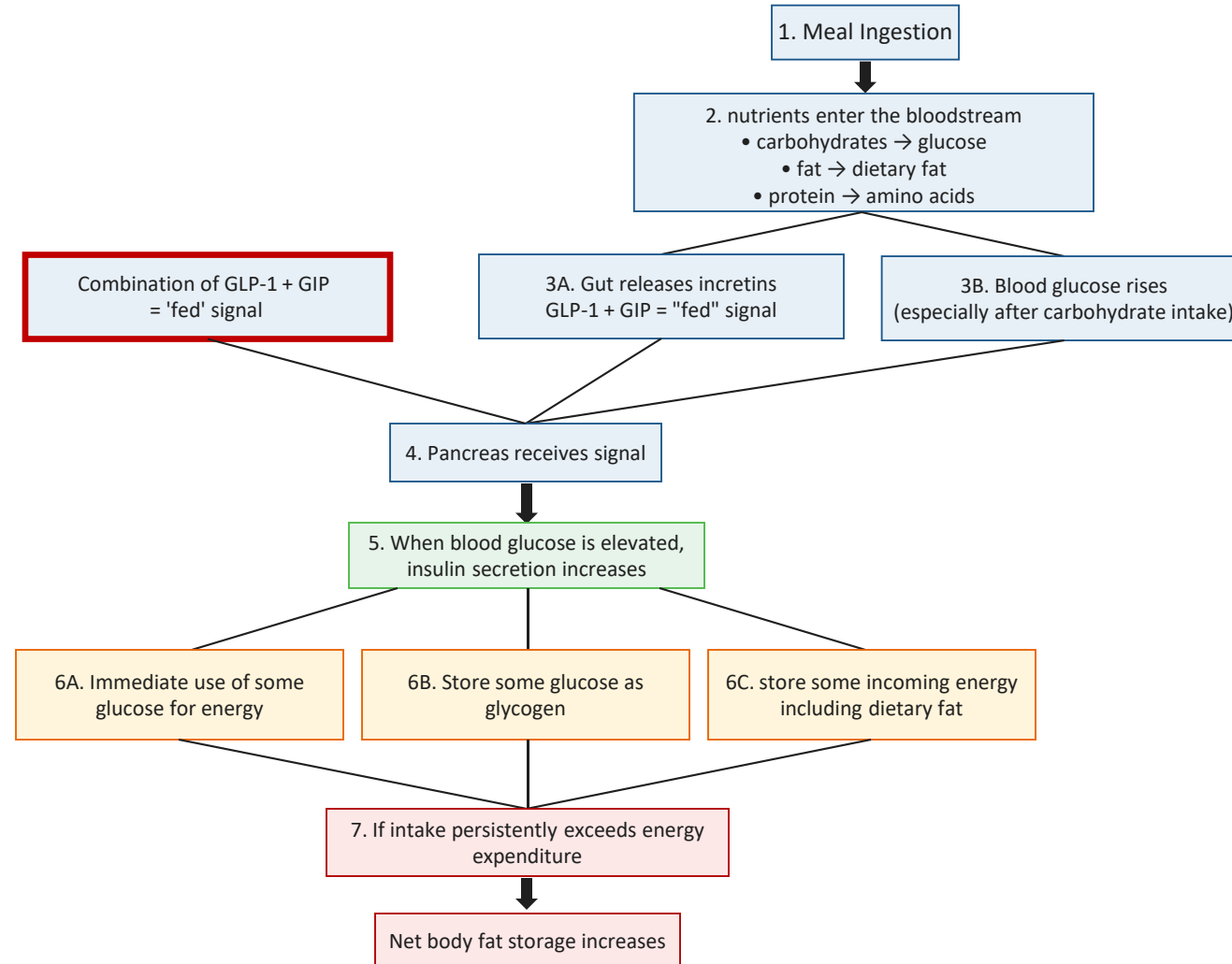
- **Merck (MRK) — Pembrolizumab (Keytruda):** Facing US patent expiration in 2028–2029; aggressively deploying capital into subcutaneous co-formulations and strategic M&A to backfill core oncology revenue.
- **AbbVie (ABBV) — Adalimumab (Humira):** Navigated major biosimilar erosion by aggressively scaling next-generation immunology blockbusters Risankizumab (Skyrizi) and Upadacitinib (Rinvoq) to offset baseline declines.

What does the Patent Cliff Mean for Pharma & Markets?

- **US\$400bn Industry Revenue at Risk:** Over the next 8 years, unprecedented patent expirations will force major pharmaceutical players (PFE, MRK, BMY) to aggressively pursue external biotech licensing and M&A.
- **The Patent Cliff:** Originator drugs enjoy monopoly pricing power and very high margins during exclusivity. Once LOE occurs, a large influx of low-cost generics or biosimilars can rapidly enter the market, causing originator prices and sales to plummet in a short time (sometimes volumes or revenues fall by 70%-90%).
- **Strategic Capital Allocation:** To prevent patent cliffs from causing revenue collapse, biopharma majors must deploy cash flow into internal R&D and strategic M&A to fill revenue voids ahead of LOE dates.

Appendix: The Physiological Pathway from Nutrient Ingestion to Adipose Storage

Pharmacological Incretin Agonism: Inducing a "Fed" State



Note: Insulin helps regulate and store fuel after meals. Stored fat is not permanently locked; when energy intake is below energy expenditure, it can be mobilized later.

Appendix: Mechanism of weight-loss drugs - Simulating GLP-1 Release

Tricking the Brain in Multiple Stages to Mimic a Perpetual "Fed" State

The term "incretin" derives from gut-stimulated insulin secretion. Whenever food is consumed, the gut produces these **endogenous metabolic hormones**, preparing the body to process ingested nutrients.

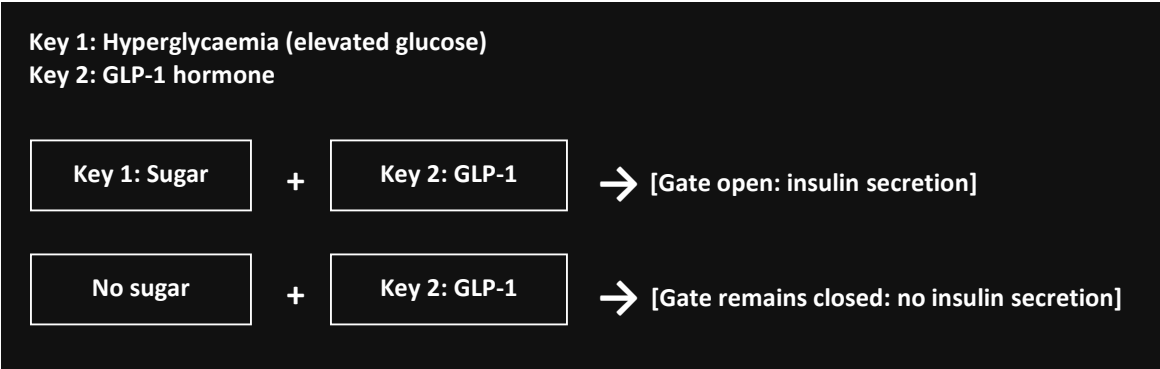
After taking GLP-1 medication, patients' 24-hour average insulin levels are lower than before treatment, reducing total daily insulin production.

Reason: Incretins only stimulate insulin when blood glucose is elevated

Because caloric intake is markedly reduced, blood glucose rarely spikes; for most of the day (including during sleeping) it remains at a lower fasting baseline. At this level, GLP-1 does not stimulate insulin secretion, sparing the pancreas from continuous high output and allowing it to rest.

Chart on the Right:

When the synthetic drug is in the body, Key 2 remains active; however, without food intake, blood glucose stays at a normal baseline (70–90 mg/dL), meaning Key 1 is absent. Without Key 1 (actual glucose in the blood), the pancreas secretes virtually no additional insulin, regardless of circulating GLP-1 drug levels.



Stage	Change	Why it helps weight management
1. Persistent meal signals	Drug activation of the GLP-1 pathway lasts far longer than the body's brief natural pulses.	No need to rely solely on between-meal willpower; appetite across the entire day or week is stabilized.
2. Appetite and satiety	Hunger decreases; smaller portions feel sufficient; food cravings and urges diminish.	Primary driver for reducing total daily caloric intake.
3. Gastric emptying	Slower digestion and delayed stomach emptying.	Post-meal satiety and physical fullness are sustained much longer.
4. Energy balance	Average caloric intake drops below total daily energy expenditure.	Forces the body to mobilize stored fat reserves to cover the energy deficit.
5. Body composition changes	Weight loss is predominantly fat mass rather than disproportionate loss of lean muscle.	These therapies target excess adipose tissue, not transient water-weight fluctuations.

Appendix: Restricting Caloric Inflow and Accelerating Lipolysis

Reduce caloric inflow and burn stored fat

Step 1: Source Control & Appetite Regulation (Whole-Food Nutrition)

Obesity is essentially the result of energy imbalance and deterioration of dietary quality: highly processed foods and refined sugars readily stimulate brain reward pathways, provoking persistent cravings ('food noise').

- **Whole foods increase satiety:** Clean eating, rich in high-quality protein and dietary fiber, naturally delays gastric emptying and stimulates endogenous satiety signals
- **Glycaemic stability and appetite:** Avoid high-glycaemic refined carbohydrates to prevent pseudo-hunger and binge eating caused by rapid glucose spikes and crashes.

Step 2: Mobilize and oxidize stored fat (exercise and cellular metabolism)

1. Reduction in total insulin levels and improved insulin sensitivity

- **Unlocking the fat-locked state:** Insulin is a hormone that promotes fat storage and suppresses fat burning; With clean eating and stable blood glucose throughout the day, total insulin secretion from the pancreas is substantially reduced.
- **Exercise improves insulin sensitivity:**
Resistance training and aerobic exercise promote direct uptake and utilization of blood glucose by muscle cells, reducing insulin resistance and maintaining a lower-insulin milieu throughout the day that facilitates lipolysis.

2. Accelerated mitochondrial oxidation in muscle

- **Active fuel uptake:** Strenuous exercise expends energy, prompting skeletal muscle and heart tissue to take up circulating free fatty acids and deliver them to cellular powerhouses (mitochondria) for oxidation.
- **Energy production and metabolism:** Fatty acids are converted within mitochondria into ATP (energy) to power physical activity; Final metabolic byproducts are likewise converted to water (excreted via sweat and urine) and carbon dioxide (exhaled through breathing during exercise).
- **Long-term metabolic benefits:** Exercise increases muscle mass and mitochondrial density, boosting resting basal metabolic rate and transforming the body into an efficient fat-burning machine that resists weight regain.



Appendix: Key Metabolic Elements — Hormones vs. Enzymes

Distinguishing Biological Messengers from Biochemical Catalysts

Name	Biochemical Classification: Hormone vs. Enzyme	Site of production	Release timing	Primary effects	Role in modern weight-loss/diabetes drugs
GLP-1	An incretin hormone	Distal small intestine/colon; L cells	Released immediately after eating	Conveys satiety to the brain; slows gastric emptying; stimulates insulin secretion.	The basis of all GLP-1 drugs (Wegovy, Ozempic) when modified, they can persist 7 days,rather than 2 minutes,to markedly suppress appetite.
GIP	An incretin hormone	Upper small intestine; K cells	Released immediately after eating	Acts synergistically with GLP-1 to stimulate insulin; promotes adipocyte lipid storage; reduces nausea.	Add dual agonism (Mounjaro,Zepbound); improves fat handling and allows higher doses with less vomiting.
Glucagon	An pancreatic hormone	Pancreas; α cells	During fasting, sleep, or when blood glucose falls	"Opposite of insulin": stimulates the liver to burn and release stored sugars and fats for energy.	Adding triple agonists ("GGG"; Retatrutide), increases metabolic rate and burns liver fat at rest.
Insulin	An pancreatic hormone	Pancreas; β cells	After meals, when blood glucose rises	"Storage key": sends glucose into muscle and locks excess energy into fat cells.	The goal is for incretin-based drugs to restore the body's ability to secrete insulin as needed without causing hypoglycaemia.
DPP-4	Not hormone but an enzyme	Systemic — in blood and on cell surfaces	Persistent	The "chemical scissors": within 1-2 minutes, cleave and destroy native GLP-1 and GIP.	Modern drugs are chemically modified so that DPP-4 cannot degrade them.

Difference between hormones and enzymes?

Hormone is the body's "chemical messenger", responsible for coordinating and directing organ function;

Enzyme is a "biological catalyst" that accelerates chemical reactions in the body.

Comparison dimensions	Hormone	Enzyme
Core role	Signal transmitter (sends instructions)	Chemical catalyst (catalyzes reactions)
Metaphor	Letters / instructions	Machine / scissors
Primary functions	Regulate physiological balance (growth, metabolism, mood, reproduction, etc.)	Accelerate specific chemical reactions (such as digestion, DNA replication)
Chemical composition	Diverse types (amino acid derivatives, peptides/proteins, steroid lipids)	The vast majority are proteins (a small minority are RNA/ribozymes)
Sites of action and transport	Secreted by endocrine glands and transported via the bloodstream to distant target organs	Within cells or at specific sites (e.g., the gastrointestinal lumen) local action
Pre- and post-reaction changes	After action, they are taken up by cells and gradually metabolized and degraded	Catalysts themselves are unchanged before and after the reaction and can be reused
Examples of incretins	GLP-1 、 GIP 、 insulin, glucagon.	DPP-4 、 lipase.

Appendix: Key Industry Terms

Pharmacological mechanisms and targets

GLP-1RA (GLP-1 Receptor Agonist)	Mimicking endogenous GLP-1 incretin hormone that promotes insulin secretion, suppresses appetite and delays gastric emptying.
GIP (Glucose-dependent Insulinotropic Polypeptide)	GIP, another incretin; when combined with GLP-1 (e.g., tirzepatide), it produces synergistic weight-loss and glycaemic control.
Glucagon / GCGR	A target that promotes hepatic lipolysis and increases basal metabolic rate (e.g., the third target of triple-receptor Retatrutide).
Amylin / Amylin Analogues	Another pancreatic satiety hormone and a core target for next-generation GLP-1 combination therapies (e.g., CagriSema).
Dual / Triple Agonist	Single drug molecules that simultaneously activate two (dual-receptor) or three (triple-receptor) receptors.
Peptide vs. Small Molecule	Peptides (large molecules) often require injection and are costly; small molecules (non-peptidic) can be taken orally and have much lower chemical synthesis costs.

Clinical and patient-experience metrics

Food noise	Intense, persistent psychological cravings and intrusive thoughts about food, GLP-1 receptor agonists can markedly abolish this phenomenon.
Weight set point	The weight set point established by the hypothalamus, GLP-1 receptor agonists can reset this set point downward.
Delayed gastric emptying	Slows the rate at which food leaves the stomach, substantially prolonging physical satiety and preventing postprandial blood glucose spikes.
Dose escalation	The process of initiating therapy at a low dose and escalating weekly/then monthly to mitigate gastrointestinal adverse effects such as nausea and vomiting.
Cardiovascular outcomes trial (CVOT)	Large trials designed to demonstrate whether the drug, beyond weight-loss and glycaemic effects, reduces hard endpoints such as heart disease and stroke.
Major adverse cardiovascular events (MACE)	A composite endpoint used in clinical trials to capture serious events such as myocardial infarction, stroke and cardiovascular death.
Metabolic dysfunction-associated steatohepatitis (MASH)	Liver inflammation and fibrosis that evolves from fatty liver; a new specialty indication that GLP-1/triple-receptor agonists are aggressively targeting.

Commercial, Supply-Chain & Regulatory Terms

New-patient prescription volume (NBRx)	Core commercial metric measuring new-prescription patient share and volume momentum, reflecting competitors' ability to capture patients.
Aseptic fill-finish	The final step of filling drug solution into auto-injectors or vials; currently the biggest global GLP-1 supply-chain bottleneck.
Wholesale list price (WAC)	Manufacturer-published wholesale acquisition price (the list price before deducting discounts and rebates given to PBM).
Patient out-of-pocket cost (OOP)	Net cash amount patients pay after health insurance or payor coverage is applied.
Pharmacy Benefit Manager (PBM)	Intermediary organizations that negotiate drug prices and establish insurance reimbursement (Formulary) on behalf of insurers within the U.S. healthcare system.
Loss of Exclusivity (LOE) / Patent Cliff	The timing when drug patents and exclusivity expire, at which point low-priced generics (Generics) will enter the market and pressure revenues.

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